STUDIES WITH ANTIGENS

VII. The Significance of Reactions to Intracutaneous Tests Performed with Extracts of Purified House Dust

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INTRODUCTION

In a previous communication (1) we reported the significance of reactions to scratch tests performed with 0.87, 0.75, and 0.50 per cent solutions of house dust purified according to the technique reported by Boatner, Efron, and Dorfman (2, 3). The incidence of positive reactions of no concurrent clinical significance was determined to be 7.00 ± 1.80 per cent to 8.50 ± 1.97 per cent. The incidence of positive reactions in patients with perennial hay fever or asthma, or both, was found to be 75.62 ± 3.39 per cent to 78.75 ± 3.24 per cent. These solutions of purified house dust were diagnostic of allergic disease attributable to house dust in 90.26 ± 2.96 per cent to 91.53 ± 2.78 per cent of instances.

These findings show that purified house dust is neither a "primary irritant" nor an irritating extract in these concentrations. Reactions to scratch tests performed with it are both allergic and diagnostic.

The purpose of this investigation is to evaluate the significance of reactions to intracutaneous tests performed with extracts of this purified house dust.

TEST METHOD

Two groups of patients were studied. The first was a control series consisting of 67 consecutive patients whose present and past histories were negative for hay

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fever, asthma, urticaria, eczema, frequent and recurrent coryza, recurrent bronchitis, and nasal obstructions, and who showed no reactions to scratch tests performed with solutions of purified house dust in the three concentrations specified above. The second series consisted of 73 consecutive patients with perennial hay fever or asthma, or both, on whom positive reactions to scratch tests were obtained with the three solutions of house dust.

The sites of injection were placed vertically on the lateral aspect of the arm, at least two inches apart. Injections were made as superficially as possible, and approximately 0.01 cc. was injected into each test site. Solutions of purified house dust of the following concentrations were used: .002, .001, .0005, .0002, .0001, .00002, .00001, .000004, and .000002 per cent. These represent serial dilutions (made with normal saline containing 0.4 per cent phenol by weight) of a 0.1 per cent solution of purified house dust in a 50 per cent glycerin solution containing 0.85 per cent sodium chloride by weight. Consequently, the .002 per cent solution of house dust contained 1.0 per cent glycerin by volume; the .001 per cent solution contained 0.50 per cent glycerin by volume; etc. The control solution consisted of 1.0 per cent glycerin by volume in a normal saline solution containing 0.4 per cent phenol by weight.

In order to avoid "contamination" from other concentrations, a designated set of syringes and needles was used for each different concentration of solution.

Readings were made at the end of twelve minutes. All tests were performed and read by the same person (B. G. E.).

Reactions were estimated as positive, doubtful, or negative. In addition to this classification, the reactions were grouped on the basis of relative size according to the following criteria:

Negative = reaction not larger than that produced by the control solution.

Doubtful = reaction questionably larger than that produced by the control solution.

Slight = reaction definitely although only slightly larger than that produced by the control solution.

Moderate = reaction definitely larger than that produced by the control solution, the wheal of the reaction having no pseudopodia.

Marked = reaction definitely larger than that produced by the control solution, the wheal of the reaction having pseudopodia.

DISCUSSION

In the control series (table 1), the incidence of reactions to tests performed with each concentration was not significantly different from that of positive reactions obtained by means of scratch tests performed with 0.87, 0.75, and 0.50 per cent solutions on the same patients. Therefore, for the two types of tests, these are analogous concentrations with respect to incidence of positive reactions of no concurrent clinical significance.

When positive scratch tests are obtained with 0.87 to 0.50 per cent solutions in patients with perennial hay fever or asthma, or

TABLE 1

Reactions to intracutaneous tests in patients in control series

SCRATCH TESTS*		INTRACUTANEOUS TESTS				P†	INTERPRETATION
Positive	Negative	Concentration of extract	Positive	Negative	Doubtful		
		per cent					
0	67	.002	2	62	3	.20	No significant difference
0	67	.001	2	62	3	.20	No significant difference
0	67	.0005	1	63	3	.49	No significant difference
0	67	.0002	1	64	2	.49	No significant difference
0	67	.0001	0	67	0	1.00	No significant difference
0	67	.00002	0	67	0	1.00	No significant difference
0	67	.00001	0	67	0	1.00	No significant difference
0	67	.000004	0	67	0	1.00	No significant difference
0	67	.000002	0	67	0	1.00	No significant difference

* Scratch tests were performed with .87, .75, and .50 per cent solutions.

† The exact probability was calculated from a tetrachoric table by combinatorial methods. The question tested is that of independence in a tetrachoric table between the two dichotomies giving rise to it. Therefore the probability calculated is that, on the null hypothesis of independence, of a discrepancy from proportionality as great as that observed or greater (4).

TABLE 2

Reactions to intracutaneous tests in patients with perennial hay fever and/or asthma and positive reactions to scratch tests

SCRATCH TESTS*		INTRACUTANEOUS TESTS				VALUE OF CHI-SQUARE†	n	P
Positive	Negative	Concentration of extract	Positive	Negative	Doubtful			
		per cent						
73	0	.002	73	0	0			1.00‡
73	0	.001	73	0	0			1.00‡
73	0	.0005	70	2	1			.20‡
73	0	.0002	69	3	1			.12‡
73	0	.0001	46	19	8	22.352	1	<.01
73	0	.00002	26	38	9	57.044	1	<.01
73	0	.00001	20	47	6	73.984	1	<.01
73	0	.000004	12	57	4	97.335	1	<.01
73	0	.000002	11	57	5	99.242	1	<.01

* Footnote*, table 1.

† For concentrations of .0001 per cent and less, the probability is approximated by the Chi-Square Test, using Yates' correction for continuity (5).

‡ Footnote†, table 1.

both, the incidence of positive reactions to intracutaneous tests performed with .002, .001, .0005, and .0002 per cent solutions

TABLE 3

Comparison of incidence of positive reactions to intracutaneous tests in patients in control series with no reactions to scratch tests with the incidence of positive reactions in patients with perennial hay fever and/or asthma with positive reactions to scratch tests

SCRATCH TESTS*	INTRACUTANEOUS TESTS			VALUE OF CHI-SQUARE†	n	P
	Concentration of extract	Positive	Negative			
	per cent					
Negative	.002	2	62	125.288	1	<.01
Positive		73	0			
Negative	.001	2	62	125.288	1	<.01
Positive		73	0			
Negative	.0005	1	63	120.462	1	<.01
Positive		70	2			
Negative	.0002	1	64	117.830	1	<.01
Positive		69	3			
Negative	.0001	0	67	69.711	1	<.01
Positive		46	19			
Negative	.00002	0	67	31.427	1	<.01
Positive		26	38			
Negative	.00001	0	67	21.208	1	<.01
Positive		20	47			
Negative	.000004	0	67	10.727	1	<.01
Positive		12	57			
Negative	.000002	0	67	9.738	1	<.01
Positive		11	57			

* Footnote*, table 1.

† The probability is approximated by the Chi-Square Test using Yates' correction for continuity.

(table 2), is not significantly different from the incidence of positive reactions to scratch tests. Therefore, for the two types of

tests, these are analogous concentrations with respect to clinically significant reactions. When positive scratch tests are obtained with 0.87 to 0.50 per cent solutions in patients with perennial hay fever, asthma, or both, the incidence of positive reactions to intracutaneous tests performed with solutions of .0001 per cent concentration or less (table 2) is significantly

TABLE 4

Size of reactions

CONCENTRATION OF EXTRACT		MARKED	MODERATE	SLIGHT	DOUBTFUL	NEGATIVE	TOTAL
per cent							
.002	I*	0	2	0	3	62	67
	II*	45	28	0	0	0	73
.001	I	0	2	0	3	62	67
	II	30	42	1	0	0	73
.0005	I	0	0	1	3	63	67
	II	10	57	3	1	2	73
.0002	I	0	0	1	2	64	67
	II	8	57	4	1	3	73
.0001	I	0	0	0	0	67	67
	II	1	25	19	8	20	73
.00002	I	0	0	0	0	67	67
	II	0	9	17	9	38	73
.00001	I	0	0	0	0	67	67
	II	0	9	11	6	47	73
.000004	I	0	0	0	0	67	67
	II	0	5	7	4	57	73
.000002	I	0	0	0	0	67	67
	II	0	3	9	5	56	73

* I. Control series: no reaction to scratch tests.

II. Series with perennial hay fever and/or asthma: positive reactions to scratch tests.

smaller than the incidence of positive reactions to scratch tests. Therefore, for the two types of tests, solutions of .0001 per cent or less are relatively weaker with respect to clinically significant reactions.

The small incidence of positive reactions in patients of the control series and the significantly greater incidence of positive reactions to each concentration of the extract in patients with

hay fever and/or asthma than in control cases (table 3), show that concentrations of .001 to .000002 per cent are not irritating and that the reactions are allergic in character (1).

The incidence of positive reactions to intracutaneous tests performed with .002 to .0002 per cent solutions, which are diagnostic of allergic disease attributable to house dust, is at least equal to the incidence of positive scratch tests performed with 0.87 to 0.50 per cent solutions. This conclusion is warranted from the following observations:

1. The incidence of positive reactions in patients in the control series to tests performed with the .002 to the .0002 per cent solutions is not significantly different for intracutaneous tests performed with these concentrations and for scratch tests performed with the 0.87 to 0.50 per cent solutions on the same patients (table 1).

2. The incidence of positive reactions to intracutaneous tests in patients with perennial hay fever and/or asthma performed with .002 to .0002 per cent solutions is not significantly different from the incidence of positive reactions to scratch tests when positive scratch tests are obtained with 0.87, 0.75, and 0.50 per cent solutions (table 2).

Table 4 presents the positive reactions to intracutaneous tests, classified according to relative size. Marked reactions are entirely absent in the control group, in contrast to their high incidence with the .002 and the .001 per cent solutions, and to their presence with the .0005 and the .0002 per cent solutions in patients with perennial hay fever or asthma, or both.

SUMMARY

1. The incidence in the control series of positive reactions to intracutaneous tests performed with solutions of purified house dust of .002 per cent concentration or less is not significantly different from the incidence of reactions to scratch tests performed with 0.87, 0.75, and 0.50 per cent solutions of the same substance. Therefore, for the two types of tests, these are analogous concentrations with respect to the incidence of positive reactions of no concurrent clinical significance.

2. When positive scratch tests are obtained with 0.87, 0.75, and 0.50 per cent solutions in patients with perennial hay fever or asthma, or both, the incidence of positive reactions to intracutaneous tests performed with .002 to .0002 per cent solutions is not significantly different from the incidence of positive reactions to scratch tests. Therefore, for the two types of tests, these are analogous concentrations with respect to the incidence of clinically significant reactions.

3. When positive scratch tests are obtained with 0.87, 0.75, and 0.50 per cent solutions in patients with perennial hay fever or asthma, or both, the incidence of positive reactions to intracutaneous tests performed with .0001 to .000002 per cent solutions is significantly smaller than the incidence of positive reactions to scratch tests. Therefore, concentrations of .0001 to .000002 per cent are relatively weaker with respect to the incidence of clinically significant reactions.

4. Extracts of purified house dust up to and including .002 per cent solutions are not irritating.

5. The reactions produced by solutions of purified house dust up to and including concentrations of .002 per cent are allergic in character.

6. The incidence of positive reactions to intracutaneous tests performed with .002 to .0002 per cent solutions of purified house dust, which are diagnostic of allergic diseases attributable to house dust, is at least equal to the incidence of positive diagnostic reactions to scratch tests performed with 0.87 to 0.50 per cent solutions.

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